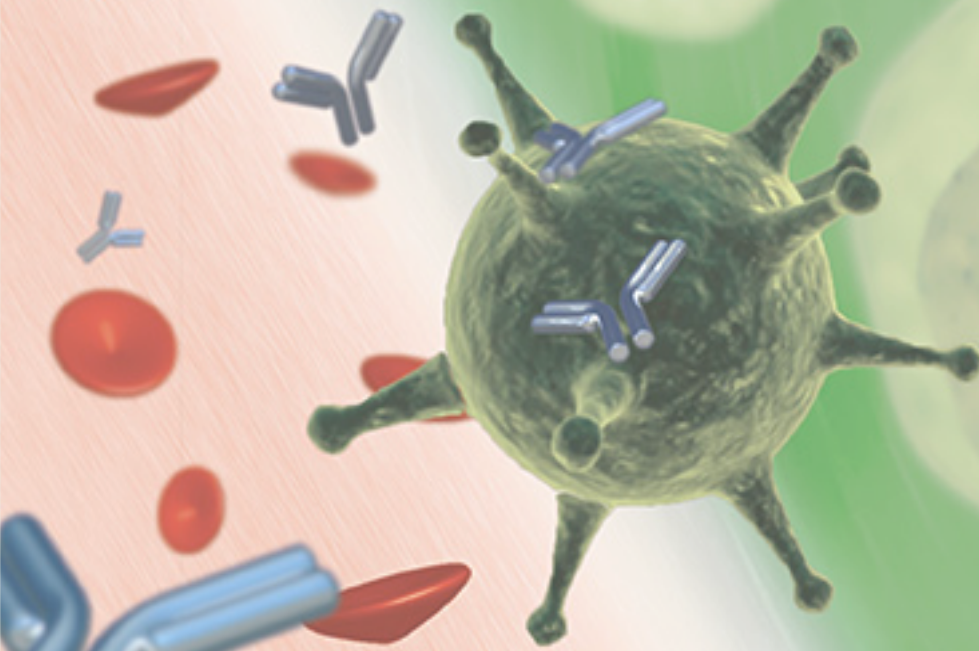




From Research to Discovery

Innate Immunity



Inflammasomes & TLR Signalling

Innate Immunity-related products from Covalab

Innate Immunity

Innate immunity corresponds to the non-specific response of the organism to pathogens and is mediated by mast cells, phagocytes (macrophages, neutrophils and dendritic cells), basophils, eosinophils, NK cells as well as $\gamma\delta$ T cells. This first line of defence is found in all class of plants and animals (vertebrate or not). It is based on the recognition of Pathogen-Associated Molecular Patterns (PAMPs) or endogenous danger signals through the sensing of Danger-Associated Molecular Patterns (DAMPs) by pattern recognition receptors¹ (PRRs). Activation of PRRs triggers cell signalling leading to the production of proinflammatory cytokines, chemokines and type 1 interferons, the induction of antimicrobial and inflammatory responses, pyroptotic cell death and the recruitment of phagocytic cells. These innate responses are responsible for efficient destruction and clearance of invading pathogens and other molecular threats and instructing the development of an appropriate pathogen-specific adaptive immune response.

Innate immune system comprises several classes of PRRs that allow the early detection of pathogens at the site of infection. The membrane-bound Toll-like receptors (TLRs) and C-type lectin receptors² (CLRs) detect PAMPs in extracellular and endosomal compartments. TLRs and CLRs cooperate with PRRs sensing the presence of cytosolic nucleic acids like RIG-I like helicases/receptor (RLH/RLR). Another set of intracellular sensing PRRs are NOD-like receptors (NLRs) able to recognise PAMPs and DAMPs³.

Upon stress (including infection and metabolic deregulation), certain NLRs form high molecular weight complexes called inflammasomes. These complexes associated with autophagy play a central role in controlling innate and adaptive immunity.

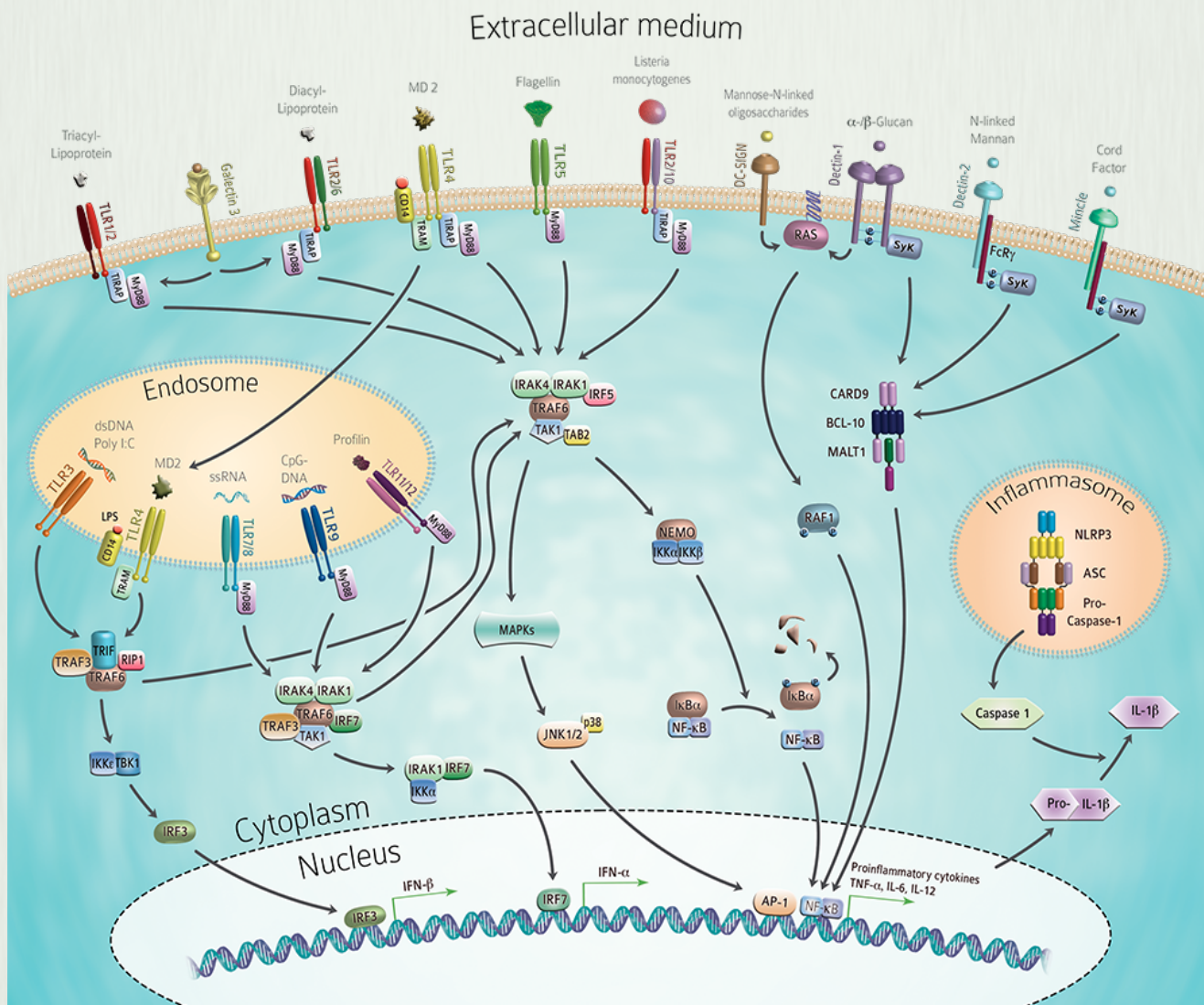


Figure 1: Schematic and simplified PRRs signalling overview

Inflammasomes are multi-protein complexes whose activity has been implicated in physiological and pathological inflammation. The hallmarks of inflammasome activation are the secretion of the mature forms of caspase-1 and interleukin-1 β (IL-1 β) from cells of the innate immune system⁴.

An inflammasome represents a high molecular weight complex that activates inflammatory caspases and cytokines of the IL-1 family (IL-1 β , IL-18 and depending on the stimulus also IL-1 α). Several inflammasomes which contain different sensor proteins such as NLRP1 (NALP1), NLRP3 (NALP3), IPAF (NLRC4), NLRP6 (NALP6), RIG-I and AIM-2 (absent in melanoma 2) have been described. Most of these inflammasomes require the adapter protein Asc (apoptosis-associated speck-like protein containing a caspase recruitment domain) to recruit caspase-1 to the inflammasome complex. Upon binding to the inflammasome, caspase-1 is cleaved and activated, leading to cleavage of its various targets and causing maturation and secretion of the pro-inflammatory IL-1 β . Inflammasomes can be activated through multiple signals including live bacteria, microbial toxins, xeno-compounds, cytoplasmic pathogen-associated molecular patterns (PAMPs) and/or endogenous danger signals (DAMPs)⁵.

NOD-Like Receptors (NLRs)

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
NLRC4	Rabbit	Hu	WB	pab52054
NLRC4 (C-Terminus)	Rabbit	Hu	ICC, IHC - P, WB	pab71837
NLRP1 (N-Terminus)	Rabbit	Hu	WB	pab10143
NLRP1 (C-Terminus)	Rabbit	Hu	ICC, IHC - P, WB	pab75348
NLRP3 (<i>clone Cryo-1</i>)	Mouse	Ms	WB	mab10107
NLRP3 (<i>clone Nalpy3-b</i>)	Mouse	Hu	IHC - F, IHC - P, IP, WB	mab71284
NLRP3 (N-Terminus)	Rabbit	Hu, Ms	ELISA, IF, IHC - P, WB	pab71843
NLRP3 (Internal)	Goat	Hu, Ms, Rat ...	ELISA, IHC - P	pab72167
NLRP3 (C-Terminus)	Goat	Hu, Rat, Bov	ELISA, IHC - P	pab72166
NLRP6 (<i>clone Clint-1</i>)	Mouse	Hu	IHC, WB	mab10165
NLRP7 (N-Terminus)	Rabbit	Hu	ELISA, IHC - P, WB	pab71844
NLRP8 (N-Terminus)	Rabbit	Hu	ELISA, IHC - P, WB	pab71845
NLRP10 (N-Terminus)	Rabbit	Hu	ELISA, IHC - P, WB	pab71839
NLRP11 (C-Terminus)	Rabbit	Hu	ELISA, IHC - P, WB	pab71840
NLRP12 (N-Terminus)	Rabbit	Hu	IP, WB	pab10153
NLRP13 (N-Terminus)	Rabbit	Hu	ELISA, IHC - P, WB	pab71841
NLRP14 (N-Terminus)	Rabbit	Hu, Ms, Rat	ELISA, IHC - P, WB	pab71842
NOD1	Rabbit	Hu	ICC, IF, IHC - P, WB	pab75966
NOD1 (N-Terminus)	Rabbit	Hu	WB	pab10149
NOD1 (C-Terminus)	Rabbit	Hu, Ms, Rat	ELISA, IHC - P, WB	pab71853
NOD1 (aa924-953)	Rabbit	Hu	FC, IHC - P, WB	pab76137
NOD1 (aa930-949)	Rabbit	Hu	IHC - P, WB	pab74794
NOD2 (<i>clone 26mNOD2</i>)	Rat	Ms	IHC - P, WB	mab71300
NOD2 (<i>clone 2D9</i>)	Mouse	Hu, Ms	IHC - P, IP, WB	mab50075
NOD2 (<i>clone 2D9</i>) [Biotin]	Mouse	Hu, Ms	IHC - P, IP, WB	mab50329
NOD2 (<i>clone 2D9</i>) [HRP]	Mouse	Hu, Ms	IHC - P, IP, WB	mab50332
NOD2 (<i>clone 2D9</i>) [DyLight 488]	Mouse	Hu, Ms	IHC - P, IP, WB	mab50331
NOD2 (<i>clone 2D9</i>) [DyLight 550]	Mouse	Hu, Ms	IHC - P, IP, WB	mab50333
NOD2 (<i>clone 2D9</i>) [DyLight 650]	Mouse	Hu, Ms	IHC - P, IP, WB	mab50330
NOD2	Rabbit	Hu	WB	pab50153
NOD2 (N-Terminus)	Rabbit	Hu	ELISA, ICC, IHC - P, WB	pab71855
NOD2 (C-Terminus)	Rabbit	Hu	ELISA, ICC, IHC - P, WB	pab71854
NOD2 [Biotin]	Rabbit	Hu	WB	pab52080
NOD2 [HRP]	Rabbit	Hu	WB	pab52083
NOD2 [DyLight 488]	Rabbit	Hu	WB	pab52082
NOD2 [DyLight 550]	Rabbit	Hu	WB	pab52084
NOD2 [DyLight 650]	Rabbit	Hu	WB	pab52081

Rig-Like Helicases (RLHs) - Antiviral signalling

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Cardif (<i>clone Adri-1</i>)	Mouse	Hu	ICC, IHC, IP, WB	mab10105
MDA5 (<i>clone Hely-1</i>)	Mouse	Hu	ELISA, IP, WB	mab10122
MDA5	Rabbit	Ms	IHC, WB	pab10141
MDA5 (Internal)	Rabbit	Hu, Ms	IHC - P, WB	pab71721
MDA5 (C-Terminus)	Rabbit	Hu, Ms	IHC - P, WB	pab71720
NS3 (<i>clone 1B6</i>)	Mouse	HepV	ICC, WB	mab10102
NS5B (<i>clone 5B-12B7</i>)	Mouse	HepV	B/N, ICC, IP	mab10104
NS5B (<i>clone 5B-3B1</i>)	Mouse	HepV	WB	mab10103
RIG-I (<i>clone Alme-1</i>)	Mouse	Hu, Ms	IHC, IP, WB	mab10110
RIG-I (<i>clone Alme-1</i>) [Biotin]	Mouse	Hu, Ms	IHC, IP, WB	mab10111
RIG-I	Goat	Hu	IHC - P	pab72837
RIG-I	Goat	Hu	IHC - P	pab72882
RIG-I (aa200-250)	Rabbit	Hu, Mk	IHC - P, WB	pab75538

Cytosolic DNA sensors

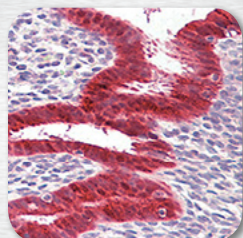
TARGET	HOST	SPECIES	APPLICATIONS	CAT #
AIM2 (C-Terminus)	Goat	Hu	ELISA, IHC - P, WB	pab73842
IFI16	Rabbit	Hu	IHC - P	pab71491
ZBP1 (<i>clone Zippy-1</i>)	Mouse	Hu, Ms	IP, WB	mab10112
ZBP1 (C-Terminus)	Rabbit	Hu, Ms, Rat	ELISA, IHC - P, WB	pab74414

Cytosolic PAMPs sensors

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Caspase-4	Rabbit	Hu, Ms	IHC - P, WB	pab70523
Caspase-4 (N-Terminus)	Rabbit	Hu, Ms	IHC, IHC - P, WB	pab70522
Caspase-4 (Internal)	Rabbit	Hu	IHC - P, WB	pab70521
Caspase-4 (aa1-89)	Chicken	Hu	IHC - P, WB	pab74177

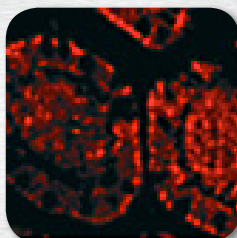
TARGET	SPECIES	APPLICATIONS	CAT #
Caspase-4	Hu	ELISA	kit20033

RIG-1
pab75538



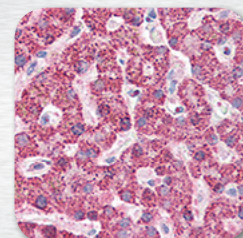
Anti-RIG-1 antibody IHC staining of human uterus.

ZBP1
pab74414



Anti-ZBP1 antibody IF staining of human small intestine cells.

MDA5
pab71721



Anti-MDA5 antibody IHC staining of human liver.

PRRs signalling

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
AKIRIN2 (Internal)	Rabbit	Hu, Ms, Rat	IHC - P, WB	pab70306
DHX58 (Internal)	Rabbit	Hu, Ms, Rat	ELISA, IHC - P, WB	pab70768
MyD88	Rabbit	Hu, Ms, Rat, Mk	ELISA, ICC, IF, WB	pab0972-P
MyD88 (Internal)	Rabbit	Hu, Ms	IHC, WB	pab60228
MyD88 (C-Terminus)	Rabbit	Hu, Ms	WB	pab60227
MyD88 (aa233-248)	Rabbit	Hu	IHC - P, WB	pab71796
MyD88 (aa233-248)	Rabbit	Hu, Ms	IHC - P, WB	pab74481
PYCARD	Rabbit	Hu	ICC, WB	pab60028
PYCARD (C-Terminus)	Goat	Hu	ELISA, IHC - P, WB	pab73143
PYCARD (aa10-59)	Rabbit	Hu, Ms, Rat	ELISA, IHC - P, WB	pab76239
PYCARD (aa182-195)	Rabbit	Hu	ICC, IHC - P, WB	pab72671
PYCARD (aa31-46)	Rabbit	Hu	IHC - P, WB	pab74592
Pyrin (N-Terminus)	Rabbit	Hu	IP, WB	pab10152
TIRAP	Rabbit	Hu	IHC - P, WB	pab75032
TIRAP (N-Terminus)	Rabbit	Hu	ELISA, IHC - P, WB	pab72227
TIRAP (C-Terminus)	Rabbit	Hu, Ms, Rat	IHC - P, WB	pab74883
TRAM (N-Terminus)	Rabbit	Hu	WB	pab10147
TRAM (C-Terminus)	Rabbit	Hu	IHC - P, WB	pab75487
TRIF (N-Terminus)	Rabbit	Hu	IP, WB	pab10145
TRIF (C-Terminus)	Rabbit	Hu	IHC - P, WB	pab74882
TRIF (C-Terminus)	Rabbit	Hu	IHC - P, WB	pab75129

NAME	HOST	SPECIES	CAT #
POP1	<i>E. coli</i>	Hu	pro10376

HMGB1: a danger stimulus for TLR2 and TLR4

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
HMGB1 (clone 1B11)	Mouse	Hu	ELISA, IF, IHC - P, WB	mab70620
HMGB1 (clone 1D5)	Mouse	Hu	ELISA, IF, IHC - P, WB	mab70619
HMGB1 (clone 2F6)	Mouse	Hu	ELISA, IF, IHC - P, WB	mab70621
HMGB1 (clone IMG19N10B7)	Mouse	Hu, Ms	FC, IHC - P, WB	mab71551
HMGB1 (clone IMG19N10B7)	Mouse	Hu, Ms	FC, IHC - P, WB	mab71636
HMGB1 (clone IMG19N15F4)	Mouse	Hu, Ms	FC, IHC - P, WB	mab71637
HMGB1	Rabbit	Hu, Ms, Rat ...	FC, ICC, IF, IHC, WB	pab50198
HMGB1	Rabbit	Hu, Po	IHC - P, WB	pab75204
HMGB1 (Internal)	Rabbit	Hu, Ms, Rat	ELISA, IHC - P, WB	pab73972
HMGB1 (Monomethyl K42)	Rabbit	Hu	ELISA, IHC, WB	pab0219
HMGB1 [Biotin]	Rabbit	Hu, Ms, Rat ...	IHC - P, WB	pab50652
HMGB1 [HRP]	Rabbit	Hu, Ms, Rat ...	IHC - P, WB	pab50655
HMGB1 [DyLight 488]	Rabbit	Hu, Ms, Rat ...	IHC - P, WB	pab50654
HMGB1 [DyLight 550]	Rabbit	Hu, Ms, Rat ...	IHC - P, WB	pab50656
HMGB1 [DyLight 650]	Rabbit	Hu, Ms, Rat ...	IHC - P, WB	pab50653
HMGB1 (recombinant antibody)	HEK293 (human transgene)	Hu, Ms, Rat	ELISA, WB	rec10002
HMGB1 (recombinant antibody) [Biotin]	HEK293 (human transgene)	Hu, Ms, Rat	ELISA, WB	rec10003

HMGB1: danger stimulus for TLR2 and TLR4 (continued)

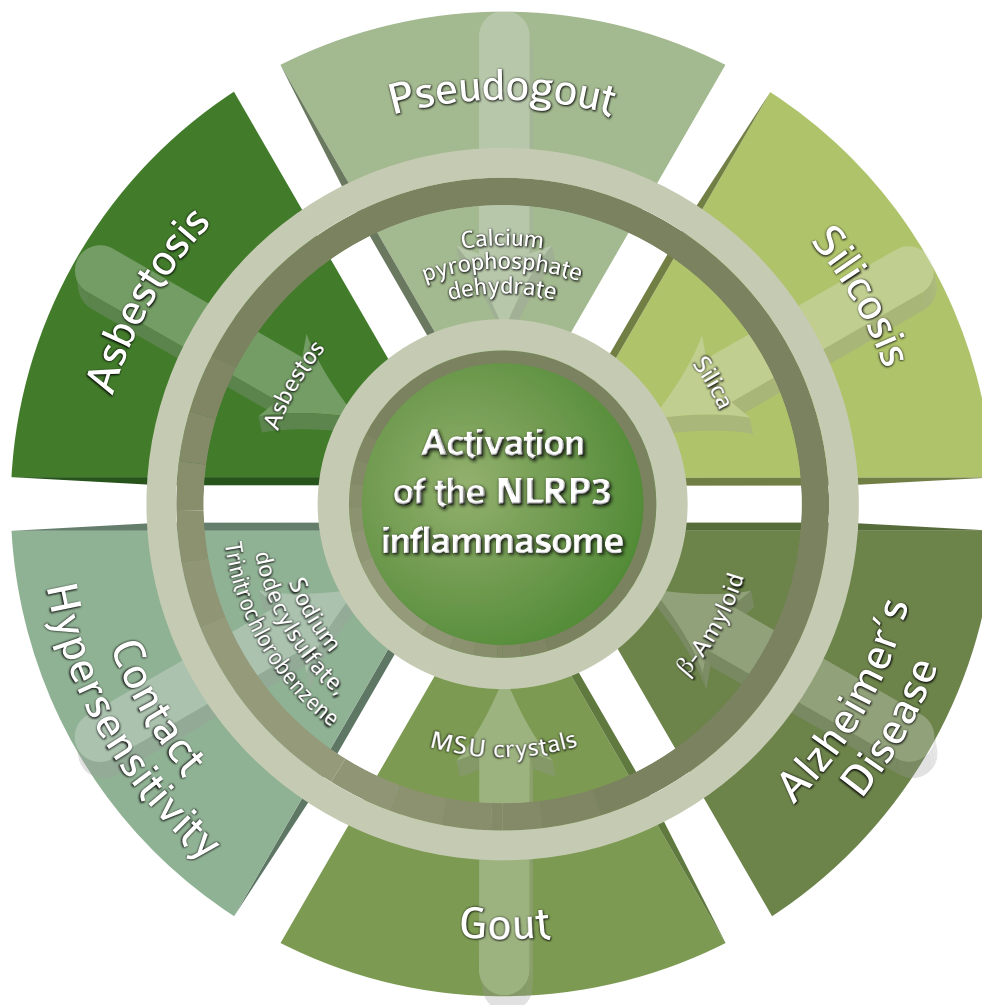
NAME	HOST	SPECIES	CAT #
HMGB1	<i>E. coli</i>	Hu	pro10093
HMGB1	CHO cells	Rat	pro10120
HMGB1	<i>E. coli</i>	Rat	pro10121



2 Inflammation Regulation

The exact sequence of events leading to activation of inflammasomes is not clear for all types of inflammasomes. The most prominent function of the NLRP3 inflammasome is the processing and activation of pro-interleukin-1 β (pro-IL-1 β). Yet most cells do not express pro-IL-1 β and thus prior expression of pro-IL-1 β is required. This can be achieved by stimulating receptors such as TLRs (e.g. LPS), NODs or TNF-Rs (e.g. TNF- α) that activate NF- κ B and initiate pro-IL-1 β transcription. This process of pro-IL-1 β induction is called priming (signal 1). Priming also induces NF- κ B-dependent transcription of NLRP3.

An additional stimulus (signal 2) results in the activation of the NLRP3 inflammasome and subsequent initiation of downstream signalling. In the absence of priming, NLRP3 inflammasome-dependent caspase-1 activation can also be observed, but IL-1 β secretion is absent^{+6 (for review), 7}.



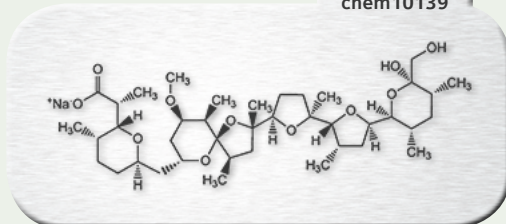
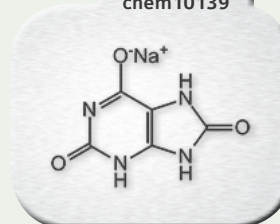
Inflammasome "priming" activators

NAME	HOST	SPECIES	CAT #
TNF-alpha (<i>soluble</i>)	E. coli	Hu, Ms	pro10238
MegaTNF-alpha (<i>soluble</i>)	HEK 293 cells	Hu, Ms	pro10304



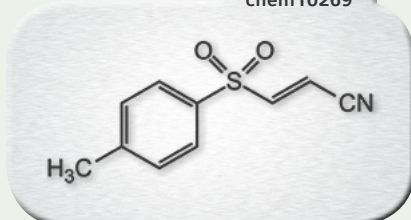
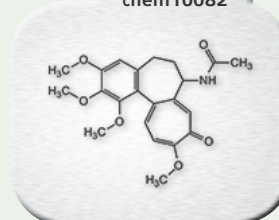
NLRP3/NALP3 inflammasome activators

NAME	CAS Number	CAT #
Monosodium urate [MSU] (<i>crystals</i>)	1198-77-2	chem10331
Monosodium urate [MSU] (<i>ready-to-use</i>)	1198-77-2	chem10332
Nigericin (<i>sodium salt</i>)	28643-80-3	chem10139

Nigericin
chem10139Monosodium urate
chem10139

Inflammasome inhibitors

NAME	CAS Number	CAT #
BAY 11-7082	19542-67-7	chem10269
Colchicine	64-86-8	chem10082

BAY 11-7082
chem10269Colchicine
chem10082

Interferon- γ (IFN- γ) is a major cytokine that is critical for host resistance to a broad range of intracellular pathogens. Production of IFN- γ by natural killer and T-cells is initiated by the recognition of pathogens by Toll-like receptors (TLRs), a first line defence against host pathogens. C.R. Sturge *et al.* recently discovered that neutrophils are a crucial source for IFN- γ that is required for TLR-independent host protection against intracellular pathogens. This finding indicates that mammals might possess a second early-alert system⁸.

Neutrophils: a TLR-independent source of IFN- γ

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Neutrophils (<i>clone Nimp-R14</i>)	Rat	Ms	FC, B/N, ICC, IHC	mab10161
Neutrophils (<i>clone Nimp-R14</i>)	Rat	Ms	FC, B/N, ICC, IHC	mab10162
Neutrophils (<i>clone Nimp-R14</i>) [Biotin]	Rat	Ms	FC, B/N, ICC, IHC	mab10163



3 Inflammasome Signalling

IL-1 β is a key player in the inflammatory response, moving inflammatory caspases and inflammasomes in an important role in several diseases (see figure 1). Several human hereditary or acquired diseases have been linked to elevated IL-1 β levels, some of which can be treated by antagonists against IL-1 β or its receptor. A number of diseases, known as cryopyrin-associated periodic syndroms (CAPS), have been directly linked to NLRP3 mutations⁹.

Gout, an autoinflammatory disease characterised by severe joint inflammation, as well as the development of type 2 diabetes mellitus (T2DM) and insulin resistance are associated to elevated IL-1 β levels. Thus by functioning as a sensor for metabolic stress, like in the form of monosodium urate (MSU) or hyperglycaemia, the NLRP3 inflammasome likely contributes to the pathogenesis of gout or T2DM, respectively¹⁰.

Several inflammasome regulators (e.g. pyrin) were shown to have a significant relevance in diseases and may allow novel entry points for disease treatment.

Caspase-1 detection

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Caspase-1 (aa371-390) (clone 14F468)	Mouse	Hu	IHC - P, WB	mab70005
Caspase-1	Rabbit	Hu	ELISA, IHC - P, WB	pab70527
Caspase-1	Rabbit	Hu, Ms, Rat	IHC, IHC - P, IP, WB	pab72774
Caspase-1 (C-Terminus)	Rabbit	Hu	ELISA, IHC, IHC - P, WB	pab70526
Caspase-1 [FITC]	Rabbit	Hu	ELISA, IHC - P, WB	pab75808

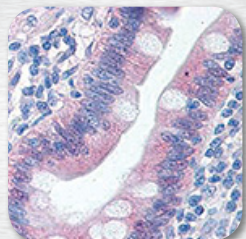
TARGET	SPECIES	APPLICATIONS	CAT #
Caspase-1	Ms	ELISA	kit10035

Caspase-1 inhibitors

NAME	CAS Number	CAT #
Q-VD-OPh	1135695-98-5	chem10227
Q-VE-OPh (Negative Control for Q-VD-OPh)		chem10320
Z-VAD-FMK (Cell permeable)	187389-52-2	chem10225

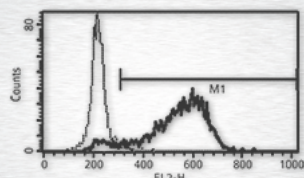
NAME	HOST	SPECIES	CAT #
Zmp1	<i>E. coli</i>	Ba	pro10417

Caspase-1
mab70005



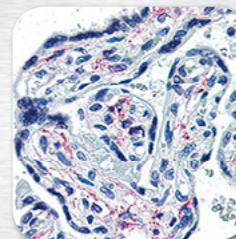
Anti-Caspase-1 antibody IHC staining of human small intestine.

IL-1 β
mab30370



Anti-IL-1 β antibody staining of LPS-activated mononuclear cells.

IL-1R1
mab70244



Anti-IL-1R1 antibody IHC staining of human placenta.

Cytokines of the IL-1 family

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
IL-1 alpha (<i>clone Bamboo-1</i>)	Mouse	Ms	ELISA, WB	mab10167
IL-1 alpha (<i>clone Bamboo-2</i>)	Mouse	Ms	ELISA	mab10169
IL-1 alpha (<i>clone Bamboo-2</i>) [Biotin]	Mouse	Ms	ELISA	mab10170
IL-1 beta (<i>clone B-A15</i>)	Mouse	Hu	FC, ELISA, ELISpot, FA	mab30201
IL-1 beta (<i>clone B-A15</i>) [PE]	Mouse	Hu	FC	mab30370
IL-1R (<i>clone IL1-31-104.1.1</i>)	Mouse	Hu	ELISA, IHC, RIA	mab60289
IL-1R (<i>clone IL1-31-113.1.1</i>)	Mouse	Hu	ELISA, IHC, RIA	mab60290
IL-1R (<i>clone IL1-31-22.2.1</i>)	Mouse	Hu	ELISA, IHC, RIA	mab60291
IL-1R1 (Extracellular Domain) (<i>clone 40101</i>)	Mouse	Hu	ELISA, IHC - P, RIA	mab70244
IL-1R2 (<i>recombinant antibody</i>)	HEK293 (mouse transgene)	Ms	ELISA, FC	rec10015
IL-1Rrp2 (aa256-286)	Rabbit	Hu	FC, IHC - P, WB	pab76033
IL-1RAcP (aa 525-540)	Rabbit	Hu, Ms, Rat	WB	pab60181
IL-1RAcP (aa 549-569)	Rabbit	Hu	WB	pab60182
IL-18	Rabbit	Hu	IHC - P, WB	pab74955

TARGET	SPECIES	APPLICATIONS	CAT #
IL-1	Hu	ELISA	kit20034
IL-1	Ms	ELISA	kit20037
IL-1 alpha	Hu	ELISA	kit30054
IL-1 alpha	Hu	ELISA	kit20035
IL-1 alpha	Ms	ELISA	kit20038
IL-1 alpha	Ms	ELISA	kit10036
IL-1 alpha (<i>pre-coated kit</i>)	Hu	ELISA	kit30174
IL-1 beta	Hu	ELISA	kit20036
IL-1 beta	Ms	ELISA	kit20039
IL-1 beta (<i>pair</i>)	Hu	ELISpot	kit30243
IL-1 beta (<i>set</i>)	Hu	ELISA	kit30055
IL-1 beta (<i>set, plate not included</i>)	Hu	ELISpot	kit30057
IL-1 beta (<i>set, non-sterile plate</i>)	Hu	ELISpot	kit30056
IL-1 beta (<i>set, sterile plate</i>)	Hu	ELISpot	kit30058
IL-1 beta (<i>pre-coated kit</i>)	Hu	ELISA	kit30175
IL-1 beta (<i>pre-coated kit</i>)	Hu	ELISpot	kit30223
IL-18	Hu	ELISA	kit20014
IL-18	Ms	ELISA	kit20040

NAME	HOST	SPECIES	CAT #
IL-1 alpha	<i>E. coli</i>	Hu	pro10018
IL-1 beta	<i>E. coli</i>	Hu	pro10019
IL-1 beta	<i>E. coli</i>	Hu	pro10307
IL-1 beta	<i>E. coli</i>	Ms	pro10343
IL-1R	HEK 293 cells	Hu	pro10308
IL-18	<i>E. coli</i>	Hu	pro10024



Pairs

- Anti-cytokine capture antibody
- Anti-cytokine biotinylated detection antibody



Sets

- Anti-cytokine capture antibody
- Anti-cytokine biotinylated detection antibody
- Streptavidin-conjugated alkaline phosphatase
- Enzyme substrate (BCIP/NBT)
- Plates (*upon request*) / Coating solutions



Kits

- Anti-cytokine capture antibody
- Anti-cytokine biotinylated detection antibody
- Streptavidin-conjugated alkaline phosphatase
- Enzyme substrate (BCIP/NBT)
- Controls (when available) and buffers
- Pre-coated PVDF-bottomed plates

4 Transmembrane PRRs

Transmembrane Toll-like receptors (TLRs) and C-type lectin receptors (CLRs) are transmembrane PRRs located on plasma or internal membranes (endosomes, endoplasmic reticulum, lysosomes).

TLRs are a family of evolutionary conserved pattern recognition receptors (PRRs) expressed by various cell types, particularly those of the innate immune system. Ten functional TLRs have been identified in humans while twelve have been identified in mice. TLRs are type I membrane glycoproteins, characterised by a cytoplasmic TIR (Toll/interleukin-1 receptor (IL-1R)) domain and a leucine-rich repeat domain. They can detect exogenous pathogen associated molecular patterns (PAMPs) such as lipopolysaccharide (LPS), lipopeptides, proteins or nucleic acids derived from bacteria, fungi, viruses or parasites, as well as endogenous, host-derived danger associated molecular patterns (DAMPs), including HMGB1 and β -defensins. The binding of an agonist to a TLR results in the dimerisation of receptor TIR domains, which leads to the differential recruitment of adapter proteins containing also a TIR domain, MyD88, MAL, TRIF and TRAM. MyD88 and TRIF allow to mediate the interaction to downstream kinases, while MAL and TRAM translocate MyD88 or TRIF to the activated TLRs. This results in the activation of a number of downstream signalling pathways, including NF- κ B, MAPK and IRF pathways. The activation of these signalling pathways results in the production and release of various cytokines and chemokines. TLRs play a crucial role in host defence and inflammation and are implicated in the pathogenesis of immune diseases and cancer.

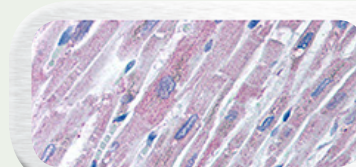
CLRs are PRRs that recognise carbohydrate ligands. The C-type designation is from their requirement for binding of calcium. This is a large family of proteins containing a signal transmembrane domain, and is divided into 17 groups based on functional and structural characteristics. Members of this receptor family contain a carbohydrate recognition domain (CRD), which mediates binding of the receptor to its carbohydrate ligand. Some of CLRs function as PRRs for the recognition of microbial components and internalise various glycoproteins and microbes for the purposes of clearance and antigen presentation to T lymphocytes. These CLRs bind to carbohydrate ligands and induce multiple signalling cascades, which lead to the activation of several transcription factors including NF- κ B and induce inflammatory responses.

Cell Surface TLRs

TLR1, 2, 4, 5, 6 and 10 are present at the cell surface and recognise bacterial and fungal products. All those TLRs are conserved in human and mice except TLR10 that is only present in humans. In mice TLR11 is expressed instead of the human TLR10.

TLR 1, 2, 6 & 10

TLR2 can associate with TLR1 or TLR6 to recognise various PAMPs including lipoproteins, peptidoglycans, mannan, lipoteichoic acids, zymosan or tGPI-mucin. TLR1 recognises Gram-positive bacteria. The heterodimer TLR1/TLR2 recognises peptidoglycan and (triacyl) lipoproteins. TLR2 recognises lipoproteins and lipopeptides. TLR10 can associate with TLR2 to recognise ligands from listeria and can also sense Influenza A virus infection.



TLR2
pab60325

Anti-TLR2 antibody IHC staining of human heart smooth muscle.

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
TLR1	Rabbit	Hu, Ms	IHC, WB	pab60323
TLR1 (N-Terminus)	Rabbit	Hu, Ms	IHC - P, WB	pab75033
TLR1 (Internal)	Rabbit	Hu	ICC, IHC - P, WB	pab74884
TLR2	Rabbit	Hu, Ms	IHC, WB	pab60325
TLR2 (N-Terminus)	Rabbit	Hu, Ms	ELISA, IHC - P, WB	pab74886
TLR6 (aa408-424) (clone 86B1153.2) [FITC]	Mouse	Hu	FC, IHC - P	mab71647
TLR6	Rabbit	Hu	IHC, WB	pab60327
TLR6 (N-Terminus)	Rabbit	Hu, Ms	ICC, IHC - P, WB	pab74888
TLR6 (Internal)	Rabbit	Hu	IHC - P, WB	pab75034
TLR10	Rabbit	Hu	IHC - P, WB	pab74885
TLR10	Rabbit	Hu	IHC - P, WB	pab75040

TARGET	SPECIES	APPLICATIONS	CAT #
TLR1	Hu	ELISA	kit20017
TLR2	Hu	ELISA	kit20018
TLR2	Ms	ELISA	kit20026
TLR2 (soluble)	Rat	ELISA	kit20031
TLR6 (soluble)	Rat	ELISA	kit20032
TLR10	Hu	ELISA	kit20025

Applications abbreviations - B/N: blocking/neutralizing assay - ELISA: enzyme-linked immunosorbent assay - ELISpot: enzyme-linked immunospot - FA: functional assay - FC: flow cytometry - ICC: immunocytochemistry - IF: immunofluorescence - IHC: immunohistochemistry - IHC - F: immunohistochemistry, frozen section - IHC - P: immunohistochemistry, paraffin section - IP: immunoprecipitation - RIA: radioimmunoassay - WB: western blot.

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TLR 1, 2, 6 & 10 — TLR 1/2 complex agonist

NAME	CAS Number	CAT #
Pam ₃ Cys-Ser-(Lys) ₄ trihydrochloride	112208-00-1	chem10319



TLR 1, 2, 6 & 10 — TLR 2/6 complex agonists

NAME	CAS Number	CAT #
FSL-1	-	chem10321
(R)-FSL-1	-	chem10322



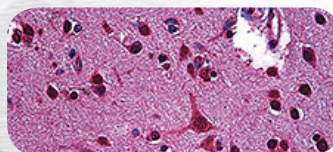
TLR 1, 2, 6 & 10 — TLR 1/2 & 2/6 coreceptor

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Galectin-3 (<i>clone 1G8</i>)	Mouse	Hu	IF, IHC - P, WB	mab71694
Galectin-3 (<i>clone B-E53</i>)	Mouse	Hu	ELISA	mab30243
Galectin-3 (<i>clone B-S43</i>)	Mouse	Hu	ELISA	mab30242
Galectin-3	Rabbit	Hu	ELISA, IHC, WB	pab0001
Galectin-3 (Internal)	Rabbit	Hu, Ms, Rat	ELISA, IF, IHC - P, WB	pab73759
Galectin-3 (Internal)	Goat	Hu, Ms	ELISA, IHC - P, WB	pab76172
Galectin-3 (aa151-251)	Rabbit	Hu, Ms	IHC - P, WB	pab75179



TLR 4

TLR4 recognises bacterial lipopolysaccharide (LPS). It can also form an heterodimer with TLR2 to promote sterile inflammation in monocytes/macrophages after an oxidised low-density lipoprotein (oxLDL) stimulation.

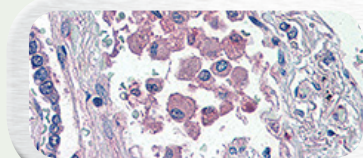
TLR4
mab71003

Anti-TLR4 antibody IHC staining of human brain, cortex.

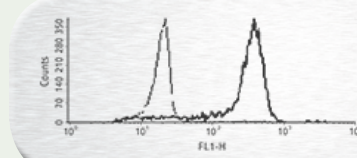
TARGET	HOST	SPECIES	APPLICATIONS	CAT #
TLR4	Mouse	Hu	ELISA, IHC - P, WB	mab71207
TLR4 (<i>clone 3B6</i>)	Mouse	Hu	ELISA, IHC - P, WB	mab71003
TLR4 (aa100-200) (<i>clone 76B357.1</i>)	Mouse	Hu, Ms, Rat	FC, IHC - P, WB	mab70179
TLR4 (Internal)	Rabbit	Hu	IHC - P	pab73624
TLR4 (Internal)	Rabbit	Hu	IHC - P	pab73626
TLR4 (C-Terminus)	Rabbit	Hu	IHC - P	pab73532
TLR4 (aa420-435)	Rabbit	Hu, Ms	ICC, IHC - P, WB	pab75568
TLR4 (aa650-700)	Rabbit	Hu, Bov, Eq, Mk	IHC - P, WB	pab75789



TARGET	SPECIES	APPLICATIONS	CAT #
TLR4	Hu	ELISA	kit20020
TLR4	Rat	ELISA	kit20028

CD14
mab71242

Anti-CD14 antibody IHC staining of human lung.

CD14
mab30126

Anti-CD14 antibody staining of monocytes.

TLR 4 agonist

NAME	CAS Number	CAT #
Kdo2-Lipid A (<i>ready-to-use</i>)	-	chem10333



TLR 4 inhibitor

NAME	HOST	SPECIES	CAT #
SIGIRR	HEK 293 cells	Hu	pro10165



TLR 4 coreceptor

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
CD14 (<i>clone 61D3</i>)	Mouse	Hu	FC, IHC - P	mab71242
CD14 (<i>clone B-A8</i>)	Mouse	Hu	ELISA, FC	mab30125
CD14 (<i>clone B-A8</i>)	Mouse	Hu	FC	mab30126
CD14 (Internal)	Goat	Hu	ELISA, IHC - P, WB	pab72606

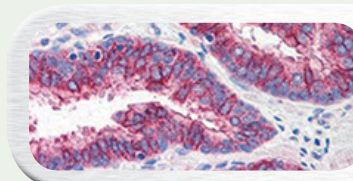


TARGET	SPECIES	APPLICATIONS	CAT #
CD14 (<i>pre-coated kit</i>)	Hu	ELISA	kit30156
Soluble CD14	Hu	ELISA	kit20041
Soluble CD14	Rat	ELISA	kit20042



TLR 5

TLR5 is highly expressed in mucosa and recognises flagellin monomers from both Gram-positive and Gram-negative bacteria. TLR5 is the only TLR to have a protein as a ligand¹².



TLR5
pab73628

Anti-TLR5 antibody IHC staining
of human prostate.

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
TLR5 (Internal)	Rabbit	Hu, Ms, Rat	IHC - P, WB	pab73628
TLR5 (C-Terminus)	Rabbit	Hu, Ms	ICC, IHC - P, WB	pab74887
TLR5 (aa300-350)	Rabbit	Hu, Ms, Rat	FC, IHC - P, WB	pab74612



TARGET	SPECIES	APPLICATIONS	CAT #
TLR5	Hu	ELISA	kit20021



TLR 5 / NLRC4 agonist

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Flagellin Fla1	Rabbit	R. homin.	ELISA, IHC, WB	pab0594
Flagellin Fla2	Rabbit	R. homin.	ELISA, IHC, WB	pab0595



NAME	HOST	SPECIES	CAT #
Flagellin	<i>Salmonella typhimurium</i> strain 14028	Hu, Ms	pro10352
Flagellin	<i>E. coli</i>	Hu, Ms	pro10378
Flagellin (<i>high purity</i>)	<i>Salmonella typhimurium</i> strain 14028	Hu, Ms	pro10309
Flagellin (<i>no association with NLRC4</i>)	<i>E. coli</i>	Hu, Ms	pro10379
Flagellin (<i>no association with TLR5</i>)	<i>E. coli</i>	Hu, Ms	pro10380



Intracellular TLRs

Intracellular TLRs are localised in endosomes and include TLR3, TLR7, TLR8, TLR9, TLR11 (expressed only in mice), TLR12 and TLR13. They recognise nucleic acids from bacteria and viruses in physiological conditions but can also recognise self-nucleic acids in auto-immune pathological conditions¹³.

TLR3 recognises double stranded DNA (dsDNA) from viruses but also small interfering RNAs and self RNAs derived from damaged cells^{14, 15, 16}.

TLR7 and TLR9 are expressed in plasmacytoid dendritic cells (pDC). TLR7 can recognise virus single stranded RNA (ssRNA) but also RNA from Streptococcus B bacteria in conventional DCs whereas TLR9 can sense viral and bacterial DNA rich in unmethylated CpG-DNA motifs but also hemozoin from *Plasmodium falciparum*¹⁷.

TLR8 recognises viral and bacterial RNA and TLR13 seems to react with bacterial 23S rRNA as well as unknown components of VSV (Vesicular Stomatitis Virus).

TLR 3, 7, 8 & 9

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
TLR3	Rabbit	Hu	ICC, IF, IHC - P, WB	pab73359
TLR3	Rabbit	Hu, Ms, Rat ...	FC, IHC - P, WB	pab75565
TLR3	Rabbit	Hu, Ms	IHC, WB	pab60326
TLR3 (N-Terminus)	Rabbit	Hu, Ms	IHC - P, WB	pab75068
TLR3 (C-Terminus)	Rabbit	Hu, Ms	ELISA, ICC, IHC - P, WB	pab74969
TLR7	Rabbit	Hu, Ms	ICC, IHC - P, WB	pab74889
TLR7	Rabbit	Hu, Ms, Rat ...	IHC - P, WB	pab50378
TLR7 (aa465-483)	Rabbit	Hu, Ms	IHC - P, WB	pab74593
TLR7 (aa706-728)	Rabbit	Hu, Ms	FC, IHC - F, IHC - P, WB	pab74552
TLR7 (aa900-950)	Rabbit	Hu, Ms, Rat ...	IHC - P, WB	pab74594
TLR8 (aa750-850) (clone 44C143)	Mouse	Hu, Ms	FC, IHC - P, WB	mab70204
TLR8	Rabbit	Hu, Ms	ICC, IHC - P, WB	pab73631
TLR8	Rabbit	Hu, Ms	IHC, ELISA, WB	pab60328
TLR8 (N-Terminus)	Rabbit	Hu	IHC - P	pab73629
TLR8 (Internal)	Rabbit	Hu, Ms	ELISA, IHC - P, WB	pab70136
TLR9 (clone 72-1665)	Rat	Hu	FC, IHC - P, WB	mab71358
TLR9 (aa268-284) (clone 26C593.2)	Mouse	Hu, Ms, Rat	FC, IHC, IHC - F, IHC - P, WB	mab70209
TLR9	Rabbit	Hu	IHC - P, WB	pab73892
TLR9 (N-Terminus)	Goat	Hu, Ms	ELISA, ICC, IHC - P, WB	pab73605
TLR9 (Internal)	Rabbit	Hu, Ms, Rat	IHC - P, WB	pab73634
TLR9 (C-Terminus)	Rabbit	Hu, Ms	IHC - P, WB	pab75134

TARGET	SPECIES	APPLICATIONS	CAT #
TLR3	Hu	ELISA	kit20019
TLR3	Rat	ELISA	kit20029
TLR7	Hu	ELISA	kit20022
TLR7	Ms	ELISA	kit20027
TLR8	Hu	ELISA	kit20023
TLR9	Hu	ELISA	kit20024
TLR9	Rat	ELISA	kit20030

Multi
Packaging

Trial
25 µg

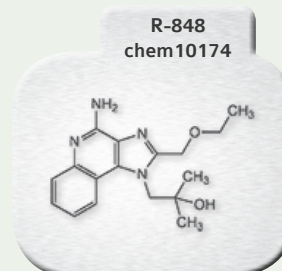
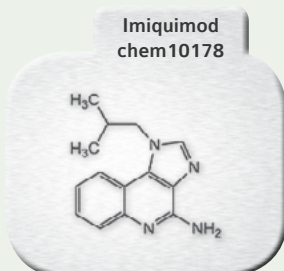
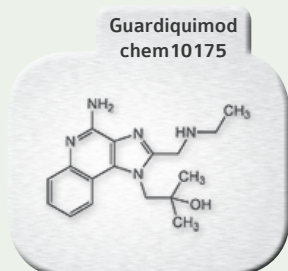
Intermediate
50 µg

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100 µg

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TLR7/8 Agonist & NLRP3 Activator

NAME	CAS Number	CAT #
Gardiquimod	1020412-43-4	chem10175
Imiquimod	99011-02-6	chem10178
Loxoribine	121288-39-9	chem10176
R-848	144875-48-9	chem10174

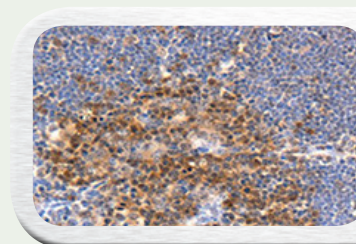


TLR3 Ligand

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Double stranded DNA (clone 11B6)	Mouse	All sp.	ELISA, IHC	mab0020
Double stranded DNA (clone AE-2)	Mouse	Hu	FC, IHC	mab71726

TLR 11 & 12 Agonists

TLR11 and TLR12 are very similar and recognise flagellin and profilin, some actin-binding proteins from diverse pathogens including *Toxoplasma gondii* or *Salmonella*¹⁸. TLR12 is predominantly expressed in myeloid cells, TLR11 is expressed only in mice - not in human - and is found at high levels in liver, bladder or kidney but weakly in spleen. This murine TLR recognises molecular patterns specific to *E. coli* uropathogenic strains.



Profilin-1
pab52329

Anti-Profilin-1 antibody IHC staining of mouse thymus.

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Profilin	Rabbit	Hu, Ms, Rat, Bov, Po	ICC, IHC, WB	pab10175
Profilin 1	Rabbit	Hu, Ms, Rat, Bov	IHC - P, WB	pab52329
Profilin 1 [Biotin]	Rabbit	Hu, Ms, Rat, Bov	IHC - P, WB	pab52330
Profilin 1 [HRP]	Rabbit	Hu, Ms, Rat, Bov	IHC - P, WB	pab52333
Profilin 1 [DyLight 488]	Rabbit	Hu, Ms, Rat, Bov	IHC - P, WB	pab52332
Profilin 1 [DyLight 550]	Rabbit	Hu, Ms, Rat, Bov	IHC - P, WB	pab52334
Profilin 1 [DyLight 650]	Rabbit	Hu, Ms, Rat, Bov	IHC - P, WB	pab52331

NAME	HOST	SPECIES	CAT #
Profilin	<i>E. coli</i>	Ms	pro10375

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Applications abbreviations - B/N: blocking/neutralizing assay - ELISA: enzyme-linked immunosorbent assay - ELISpot: enzyme-linked immunospot - FA: functional assay - FC: flow cytometry - ICC: immunocytochemistry - IF: immunofluorescence - IHC: immunohistochemistry - IHC - F: immunohistochemistry, frozen section - IHC - P: immunohistochemistry, paraffin section - IP: immunoprecipitation - RIA: radioimmunoassay - WB: western blot.

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CLRs – C-type Lectin Receptors

CLRs are PRRs that bind carbohydrates in a calcium-dependant manner. They can be divided into two groups of transmembrane receptors and one group of soluble receptors. The first group of membrane CLR (Type I) contains receptors with several CRD or CRD-like domains when Type II group of CLRs is composed of receptors with only one domain. They recognise glycan structures on pathogens and endogenous glycoproteins and facilitate the routing of internalised antigen to various MHC class I or II compartments (depending on the CLR involved) for further presentation to T lymphocytes¹⁹.

The most documented CLRs are those of the type II group that includes Dectin-1 & -2, Mincle or DC-SIGN. Dectin-1 recognises PAMPs like β -glucan in fungal cell walls and is expressed by macrophages, DCs and neutrophils. Other CLRs recognise mannan²⁰.

CLRs Detection

TARGET	HOST	SPECIES	APPLICATIONS	CAT #
Dectin-1	Mouse	Hu	IHC - P, WB	mab70005
Dectin-1 (Internal)	Rabbit	Hu	ELISA, IHC - P, WB	pab70527
DC-SIGN (Internal)	Rabbit	Hu, Ms, Rat	IHC, IHC - P, IP, WB	pab72774
DC-SIGN (Extracellular Domain)	Rabbit	Hu	ELISA, IHC, IHC - P, WB	pab70526
DC-SIGN (C-Terminus)	Rabbit	Hu	ELISA, IHC - P, WB	pab75808

TARGET	SPECIES	APPLICATIONS	CAT #
DC-SIGN	Rat	ELISA	kit20043

Caspase-1 Inhibitors

NAME	HOST	SPECIES	CAT #
Dectin-1	HEK 293 cells	Ms	pro10240
Dectin-2	HEK 293 cells	Ms	pro10241

Products



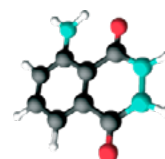
Primary Antibodies



ELISA & ELISpot kits



Purified Proteins



Chemical Compounds

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